



PATENT
CASE CD06049US01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of: :

YIN ET AL. : Examiner: B. I. Dentz

For Patent For: SYNTHESIS OF 2- : Group Art Unit: 1625
HYDROXY-N,N-DIMETHYL-3-[[2-[[1(R)-
5-METHYL-2-FURANYL)PROPYL]AMINO]- : Date: November 10, 2005
3,4-DIOXO-1-CYCLOBUTEN-1-YL]AMINO]
BENZAMIDE :

Serial No.: 10/826,456 :

Filed: April 16, 2004 :
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Schering-Plough Corporation
Kenilworth, New Jersey 07033-0530

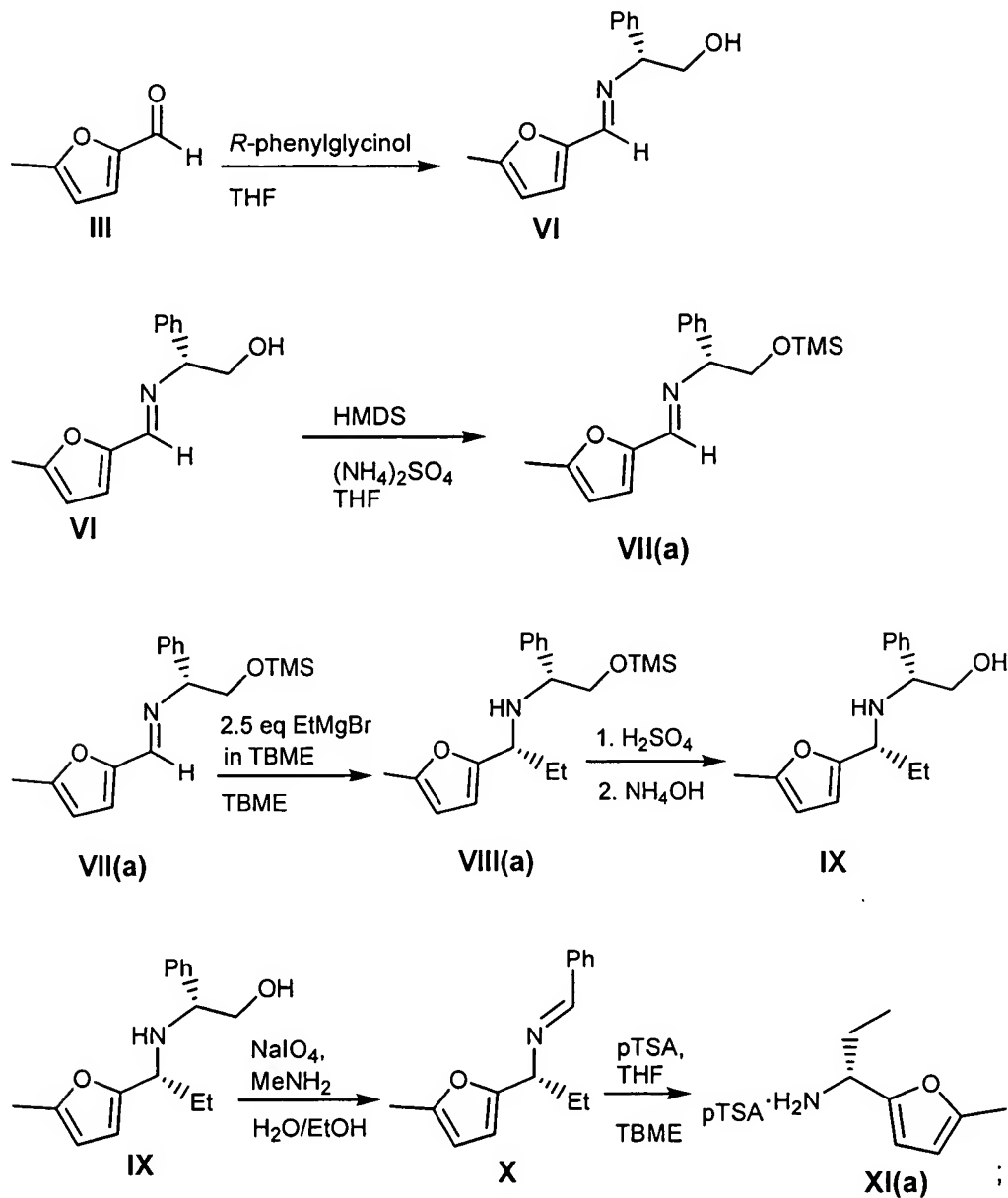
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION PURSUANT TO 37 C.F.R. 1.132

I Xiaoyong Fu hereby declare that:

1. I am an inventor of the invention claimed in the above identified Application;
2. I have a PhD in Organic Chemistry from the University of Wisconsin at Milwaukee which I obtained in 1992;
3. I have worked at Schering Corporation since 1992, and I have held the position of Development Fellow of Synthetic Chemistry at the Schering-Plough Research Institute of Schering-Plough Corporation since April 2003;
4. The process claimed in the above identified Application includes the preparation of furan imine X from the furan aldehyde III; then

Furan imine X is converted to Furan amine XI. This process is exemplified in Applicants' Scheme III (Preparative Example 1):



5. In Applicants' Preparative Example 1, the Furan aldehyde III is reacted with phenylglycinol to obtain Furan VI; Furan VI is then protected to yield Furan VII(a) which is then reacted with the organometallic reagent EtMgBr to produce Furan VIII(a); Furan VIII(a) is obtained as a mixture containing about 90% of the desired (R,R) diastereomer and about 10% of the undesired (R,S) diastereomer; Furan VIII(a) is then deprotected

to yield Furan IX; Furan IX is then subjected to oxidative cleavage with NaIO_4 to produce Furan imine X; Furan imine X is then treated with the acid pTSA to produce Furan amine XI(a);

6. In Applicants' claimed process, as exemplified in Preparative Example 1, only the desired (R,R) diastereomer is oxidatively cleaved. The undesired (R,S) diastereomer, according to HPLC analysis, remains unreacted;

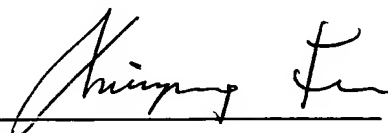
7. Because only the desired (R,R) diastereomer is cleaved, Furan XI(a) is formed in a >99% ee after the Furan imine X is treated with the acid pTSA; and

8. Obtaining Furan amine XI(a) in a purity of >99% ee was surprising and unexpected.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Further declarant sayeth not.

Nov. 10, 2005
Date


Xiaoyong Fu